UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,838	02/02/2005	Daniel W. Chan	56792(71699)	1171

49383 7590 01/05/2012

EDWARDS WILDMAN PALMER LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
DENT, ALANA HARRIS	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
01/05/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,838	CHAN ET AL.	
	Examiner	Art Unit	
	Alana Harris Dent, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *3-5,9-12,34,39,40,62 and 85-87* is/are pending in the application.

5a) Of the above claim(s) *40* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *3-5, 9-12, 34, 39, 62 and 85-87* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments and Arguments

1. Claims 3-5, 9-12, 34, 39, 40, 62 and 85-87 are pending.

Claim 40, drawn to non-elected inventions are withdrawn from examination.

Claims 3 and 40 have been amended.

Claims 85-87 have been added.

Claims 3-5, 9-12, 34, 39, 62 and 85-87 are examined on the merits.

Withdrawn Objection

Claim Objection

2. The objection to claim 3 is no longer pending because Applicants remark the claim is correct as written, see Remarks submitted October 18, 2011, page 5.

New Grounds of Objection

Claim Objections

3. Claims 3 and 85 are objected to because of the following informalities:

(a) both claims 3 and 85 cite "subject blood or tissue sample" on line 3 of each claim, however the term "subject" should be amended to "subject's" to indicate possession of the source of the blood/tissue sample; and

(b) on line 5 of claim 85 it reads "...Markers II...", however there is only one marker cited and it should read "Marker II". Correction is required.

New and Maintained Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The **NEW MATTER REJECTION** of claims 3-5, 9-12, 34, 39, 62 and new claims 85-87 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and made.

Applicants simply assert "...the method includes the use of markers individually or in combination" and indicated on page 4, 2nd paragraph, see Remarks submitted October 18, 2011, page 5. Applicants also assert support can be found in the claim as filed and the rejection should be withdrawn, see Remarks, page 5. Applicants' points of view and arguments have been carefully considered, but found unpersuasive.

The new matter issue in regard to claim 3, as well as new claim 85 is the language of the wherein clause. For claim 3 it is the phrase " "*wherein an increase in the levels of one or more of Markers II and III, or a decrease in the levels of one or more of Markers I, IV, V or VII is indicative that the subject has*

ovarian cancer" and for claim 85 the language reads "*wherein an increase in the level of Markers II and a decrease in the level of Marker VII is indicative that the subject has ovarian cancer*". Assaying one or more markers is not at the "heart" of the new matter rejection, but the method claims as a whole reading on said assay or detection step and the correlation step including the aforementioned wherein clauses. The Examiner has reviewed the specification and does not note where support for this amendment to claim 3 introduced in the "Amendments to the Claims" on February 11, 2008 is found, nor claim 85. At best the Examiner notes on page 17, lines 19-24 of the specification there is the broad contemplation of "a marker can be a polypeptide ...present at an elevated level or at a decreased level in samples...". There is no mention of specific markers that correspond to an increase or decrease in levels as set forth in claims 3 and 85. Applicants should list the page and line numbers within the disclosure that are commensurate with the new amendment or delete the new matter.

Applicants continue to not adequately respond to the Examiner's observation of the specification at page 47 that notes having three peaks with higher expression and not just one Marker or two as set forth in the claims and the citation also includes a third marker, 60kD, which is not of record in the claims. Furthermore, Applicants' specification notes the analysis uses only seven peaks, however the claims read on six, see bridging sentence of pages 47

and 48. It seems Applicants' specification only contemplates a method for detection and diagnosis of ovarian cancer implementing seven protein markers and not six as identified in claim 3 or two markers identified in claim 85. Applicants' arguments do not address the 60kD protein marker, which seems to be relevant in the claimed diagnosis and listed in the specification. The specification at page 47 notes having three peaks with higher expression *on average* and not just one Marker or two as set forth in the claims and the citation also includes a third marker, 60kD, which is not of record in the claims. The claims do not read on and average of marker levels contributing to the detection and diagnosis of ovarian cancer.

The Examiner continues to not find support for the wherein clause set forth in claim 3, as well as new claim 85, hence the rejection is maintained and made. Applicants are requested to list the page and line numbers within the disclosure that are commensurate with the amendment or delete the new matter.

6. The rejection of claims 3-5, 9-12, 34, 39, 62 and new claims 85-87 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained and made. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants assert they "...have shown the claimed methods are plainly useful to classify subjects with regard to ovarian cancer" and point out pages, Figures and Tables within the specification that support the claimed method, see page 6, last paragraph. Applicants' arguments and points of view have been carefully considered, but found unpersuasive.

The claims are directed to a method of detecting, diagnosing and staging ovarian cancer comprising measuring by mass spectroscopy at least one protein biomarker in a subject's blood or tissue sample, wherein the protein markers are 8.6kD (Marker I), 9.2kD (Marker II), 19.8kD (Marker III), 39.8kD (Marker IV), 54kD (Marker V) and 79kD (Marker VII). However, the specification does not enable one of skill in the art, at the time the invention was made, to practice the claimed methods.

Applicants' Tables 1 and 2 read on biomarkers, CA125, 60kD and Marker VII (79 kD) and while Figures 6-9 and page 48 of the specification set forth four or more biomarkers, none of these instances exemplify the claimed methods, wherein an increase in the levels of one or more of Markers II and III, or a decrease in the levels of one or more of Markers I, IV, V or VII is indicative that the subject has ovarian cancer" and for claim 85 the language reads "wherein

an increase in the level of Markers II and a decrease in the level of Marker VII is indicative that the subject has ovarian cancer".

Applicants' specification at page 47 reads "peaks at 9.2kD, 19.8kD, and 60kD showed higher expression levels *on average* among the specimens...", see last complete sentence in last paragraph. While Applicants note absolute levels of markers could be used to classify disease lines 4-6 read on two and remiss is the wherein clause language that purportedly enables assessing of one has ovarian cancer or not. There is insufficient guidance and instruction provided by Applicants, at the time of filing, as to how to correlate the listed protein markers solely identified by kD to any specific disease such as ovarian cancer encompassed by the instant claims. The information regarding the protein markers is very limited. There is no corresponding sequence, structure or identifying information.

Here, Applicant has <u>not</u> provided sufficient direction and guidance as to the sensitivity and specificity of detecting ovarian cancer using the uncharacterized protein markers alone and corresponding increases and decreases. The cutoff value for a particular assay will determine the diagnostic sensitivity and specificity of the test based on the number of individuals that are diagnosed with and without the disease.

Given the unpredictability of the art in diagnosing cancer and correlation of a set of these protein markers with any disease, and lack of guidance and

working examples in the present application, the experimentation left to those skilled in the art, would be unnecessarily, and improperly, extensive and undue.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to diagnose ovarian cancer, undue experimentation would be required to practice the claimed methods of diagnosing ovarian cancer with a reasonable expectation of success, absent a specific and detailed description in Applicants' specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for diagnosing the diseases or disorders encompassed by the claimed methods.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory

period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana Harris Dent, Ph.D. whose telephone number is (571)272-0831. The Examiner works a ***flexible schedule***, however she can generally be reached between the hours of 8 am to 6 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Misook Yu, Ph.D. can be reached on (571) 272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana Harris Dent, Ph.D.
29 December 2011

/Alana Harris Dent, Ph.D./

Primary Examiner, Art Unit 1643